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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	7

DATE MAILED: 01/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,561	MILLER ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *8-11 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 12-13, and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-23 are pending.

2. Applicant's election without traverse of Group I, claims 1-13 and 17-20 (now claims 1-13 and 17-23) drawn to a method of treating a specific neurological disorder using a polypeptide comprising SEQ ID NO: 2 that read on the species of stroke filed 11/4/02, is acknowledged.

3. Claims 1-7, 12-13, and 17-23 drawn to a method of treating a specific neurological disorder using a polypeptide comprising SEQ ID NO: 2 that read on the species of the neurological disease stroke (now claims 1-7, 12-13, and 17-23) are being acted upon in this Office Action.

4. Claims 8-11 and 14-16 that read on other neurological disease are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

5. The drawings, filed 9/27/01, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-7, 12-13, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method of making antibody that binds specifically to polypeptide comprising SEQ ID NO: 2 and a method of detecting hJIP1/IB1 of SEQ ID NO: 2 in CNS tissues, **does not** reasonably provide enablement for (1) a method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, (2) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable

carrier, (3) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (4) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in conjunction with *any* other method of treating *any* neurological disorder, (5) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by oxidative stress response in *any* neuronal tissue, (6) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of *any* polypeptide comprising *any* sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase, (7) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neuron specific, stress-activated protein kinase is c-Jun amino-terminal kinase 3, (8) the said method wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase wherein the polypeptide is administered in *any* targeted delivery system such as liposome coated with *any* antibody that specifically targets any neuronal tissue, (9) a method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2, (10) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (11) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously,

intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (12) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the method is used in conjunction with any other method of treating stroke, (13) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (14) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (15) A method of inhibiting apoptosis in human, comprising administering an effective of any polypeptide "having any sequence that is substantially equivalent" to SEQ ID NO: 2 to said human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only polypeptide comprising SEQ ID NO: 2, which corresponding to human JIP-1/IB1 and a peptide consisting of SEQ ID NO: 3. The specification defines "substantially equivalent" as any mutant sequence that varies from a reference sequence by one more amino acid substitutions, deletions, or additions...no more than about 2% differences or 98% sequence identity to SEQ ID NO: 2 (See page 11 at lines 20-28). The specification further discloses a method of inhibiting c-Jun phosphorylation by JNK3 by administering polypeptide of SEQ ID NO: 2 in vitro (See page 31, Example 3), a method of generating antibody that binds to polypeptide of SEQ ID NO: 2 by immunizing rabbit a peptide consisting of SEQ ID NO: 3 (page 31, Example 4). The specification further discloses that the antibody that binds to SEQ ID NO: 2 in human CA2 and CA3 regions of the normal hippocampus

and the Purkinjie cells in the cerebellum (See page 32). With acute hypoxia, CA1 regions of the hippocampus shows a major loss of staining of SEQ ID NO: 2, subiculum and Purkinkie cells (See Table 1). Under chronic hypoxic stress, there is a loss of cytoplasmic immunoreactivity of SEQ ID NO: 2 in Purkinjie cells. The decrease in SEQ ID NO: 2 staining in CA1 region of the hippocampus is early as 2 hours. By 4 hours, there is a more extensive loss of SEQ ID NO: 2 staining in rat Hippocampal culture plus nuclear translocation of anti-DENN/MADD staining, and apoptosis as measured by anti-ssDNA (See page 35-36).

The specification does not teach how to make *any* sequence that is substantially equivalent to SEQ ID NO: 2 because there is no guidance as to which amino acid within the full-length sequence of SEQ ID NO: 2 can be substituted, deleted, added, mutated and whether the resulting sequence after substitution, deletion, addition would have the same functions as SEQ ID NO: 2. Even if the polypeptide is limited the sequence depicted in SEQ ID NO: 2, the specification does not teach a method of treating any neurological disorder such as stroke, let alone any neurological disorder such as the ones recited in claim 17. There is no in vivo working example demonstrating any sequence that is "substantially equivalent" to SEQ ID NO: 2 or sequence comprising SEQ ID NO: 2 can treat any neurological disorder, much less stroke for the following reasons.

Habgood *et al* teach most drugs produce their pharmacological response in a concentration-dependent manner and for a drug to be effective, it needs to reach and maintain a therapeutic concentration at its target site for sufficient time to exert its effect. Habgood et al further teach yet despite the availability of a large of number of very potent drugs, many central nervous system diseases and disorders remain extremely difficult to treat due to the inability of these drugs to penetrate into the brain (See page 231, in particular). A method of treating any neurological disease in the absence of in vivo working example is unpredictable because of the following reasons: 1) the polypeptide of SEQ ID NO: 2 or equivalent thereof having 711 amino acids in length has not been demonstrated to cross the blood brain barrier; (2) even if the polypeptide cross the blood brain barrier, there is no showing in the specification as filed that the polypeptide is capable of reaching to the neuronal cell within the CA1 region of the hippocampus or the Perkinjie cell is the in the cerebellum; (3) the polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the polypeptide or the polypeptide may be adsorbed by fluids, cells and tissues where the polypeptide has no effect; and (4) other functional properties, known or

unknown, may make the polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects of inflammation of the brain prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Given the indefinite number of undisclosed polypeptide comprising any sequence having substantially equivalent to polypeptide SEQ ID NO: 2, it is unpredictable which undisclosed sequence is effective and appropriate for treating any neurological disorder such as Alzheimer's disease, stroke, amyotrophic lateral sclerosis, age associated impairment, and Parkinson's disease, much less inhibiting apoptosis in the appropriate cells within the specific region of the brain that is affected by the specific neurological disorder. Even if the polypeptide is limited to SEQ ID NO: 2, there is no showing that the claimed polypeptide can actually inhibit apoptosis. Since the method of treating a neurological disorder using any sequence substantially equivalent to SEQ ID NO: 2 or SEQ ID NO: 2 is not enabled, it follows that method wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically or in conjunction with another method is not enabled. It also follows that the method wherein neurological disorder is caused by oxidative stress response, in any neuronal tissue, or by the activation of a neuron specific stress activated protein kinase such as c-jun amino-terminal kinase 3 is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

8. Claims 1-7, 12-13, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treating *any* neurological disorder or *any* neurological disorder such as the ones recited in claims

8-9 and 17 in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, (2) the said method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (3) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (4) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in conjunction with *any* other method of treating *any* neurological disorder, (5) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by oxidative stress response in *any* neuronal tissue, (6) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of *any* polypeptide comprising *any* sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase, (7) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neuron specific, stress-activated protein kinase is c-Jun amino-terminal kinase 3, (8) the said method wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase wherein the polypeptide is administered in *any* targeted delivery system such as liposome coated with *any* antibody that specifically targets any neuronal tissue, (9) a method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2, (10) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said

human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (11) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (12) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the method is used in conjunction with any other method of treating stroke, (13) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (14) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (15) A method of inhibiting apoptosis in human, comprising administering an effective of any polypeptide "having any sequence that is substantially equivalent" to SEQ ID NO: 2 to said human.

The specification discloses only polypeptide comprising SEQ ID NO: 2, which corresponding to human JIP-1/IB1 and a peptide consisting of SEQ ID NO: 3. The specification defines "substantially equivalent" as any mutant sequence that varies from a reference sequence by one more amino acid substitutions, deletions, or additions...no more than about 2% differences or 98% sequence identity to SEQ ID NO: 2 (See page 11 at lines 20-28). The specification further discloses a method of inhibiting c-Jun phosphorylation by JNK3 by administering polypeptide of SEQ ID NO: 2 in vitro (See page 31, Example 3), a method of generating antibody that binds to polypeptide of SEQ ID NO: 2 by immunizing rabbit a peptide consisting of SEQ ID NO: 3 (page 31, Example 4). The specification further discloses that the antibody that binds to SEQ ID NO: 2 in human CA2 and CA3 regions of the normal hippocampus and the Purkinjie cells in the cerebellum (See page 32). With acute hypoxia, CA1 regions of the hippocampus show a major loss of staining of SEQ ID NO: 2, subiculum and Purkinkie cells (See Table 1). Under chronic hypoxic stress, there is a loss of cytoplasmic immunoreactivity of SEQ ID NO: 2 in Purkinjie cells. The decrease in SEQ ID NO: 2 staining in CA1 region of the

hippocampus is early as 2 hours. By 4 hours, there is a more extensive loss of SEQ ID NO: 2 staining in rat Hippocampal culture plus nuclear translocation of anti-DENN/MADD staining, and apoptosis as measured by anti-ssDNA (See page 35-36).

With the exception of the specific polypeptide comprising SEQ ID NO: 2, there is insufficient written description about the structure of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, much less having the same function as SEQ ID NO: 2, in turn, for a method of treating *any* neurological disorder such as stroke in a human patient or inhibiting apoptosis.

Further, given the lack of a written description of *any* additional representative species of polypeptide comprising a sequence substantially equivalent to SEQ ID NO: 2 as encompassed by the claims for a method of treating any neurological disorder, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "has" or "having" in claims 21-23 is indefinite and ambiguous. The Office interprets "has" or "having" as "comprising", which is open-ended. If the claimed polypeptide is intended to be open-ended, it is suggested that Applicant amends the claim to recite polypeptide "comprising".

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1-6, 12, 17-20 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/44106 (Oct 8, 1998; PTO 1449).

The WO 98/44106 publication teaches a method of treating a neurological disorder such as ischemia disease of the CNS, also known as stroke by administering a polypeptide such as IB1 (islet-brain 1) wherein the reference polypeptide is substantially equivalent with 99.7% identity (a splice variant that has additional 47 amino acids in the C terminal that contains a HLH and PID domain) to the claimed polypeptide of SEQ ID NO: 2 (See page 41, lines 33-37, claim 27 of WO 98/44106 publication, in particular) by protecting cells from apoptosis to allow cells to survive in condition such as hypoxia or low oxygen environment (See page 42, line 10-11, claim 30 of WO 98/44106 publication, page 46, line4-6, in particular). The reference method wherein the reference polypeptide IB1 is administered in a composition further comprising a pharmaceutical acceptable carrier such as physiological saline (See page 42, line 32, in particular) by administering intravenous, cutaneous or subcutaneous injection, orally, nasal, intramuscular, or intraperitoneal routes (See page 42, lines 24, lines 35 bridging page 43, lines 1-26, in particular). The reference neurological disorder such as ischemia in the CNS is inherently caused by oxidative stress response in neuronal tissue due to activation of the stress-activated protein kinase such as JNK-activated pathway since the reference polypeptide is an inhibitor of the JNK-activated pathway (See page 74, line 19, in particular). The reference polypeptide is administered in a targeted drug delivery system such as antibody or cell specific ligands (See page 43, line 27-30, in particular). The reference method can be administered in combination with other treatments, either simultaneously or sequentially (See page 44, lines 15-17, in particular). Thus, the reference teachings anticipate the claimed invention.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/44106 (Oct 8, 1998; PTO 1449) in view of Yang *et al* (Nature 389(6653): 865-70, Oct 1997; PTO 892).

The teachings of the WO 98/44106 publication have been discussed supra.

The claimed invention in claim 7 differs from the reference only that the method wherein the protein kinase is c-Jun amino-terminal kinase 3.

Yang *et al* teach c-Jun amino-terminal kinase (JNK) such as Jnk 3 is expressed in selectively expressed in the nervous system and required for stress-induced neuronal apoptosis since disruption of Jnk3 in mice prevent hippocampal neuron apoptosis from glutamate neurotoxicity (See abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inhibit apoptosis mediated by c-Jun amino-terminal kinase 3 as taught by Yang *et al* for a method of treating neurological disorder which comprises administering an effective amount of a sequence substantially equivalent to SEQ ID NO: 2 as taught by the WO 98/44106 publication. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Yang *et al* teach c-Jun amino-terminal kinase (JNK) such as Jnk 3 is selectively expressed in the

nervous system and required for stress-induced neuronal apoptosis since disruption of Jnk3 in mice prevent hippocampal neuron apoptosis in neurological disorder such as glutamate neurotoxicity (See abstract, in particular). The WO 98/44106 publication teaches a method of treating a neurological disorder such as ischemia disease of the CNS, also known as stroke by administering a polypeptide such as IB1 (islet-brain 1) wherein the reference polypeptide is substantially equivalent (a splice variant that has additional 47 amino acids in the C terminal that contains a HLH and PID domain) to the claimed polypeptide of SEQ ID NO: 2 (See page 41, lines 33-37, claim 27 of WO 98/44106 publication, in particular) by protecting cells from apoptosis to allow cells to survive in condition such as hypoxia or low oxygen environment (See page 42, line 10-11, claim 30 of WO 98/44106 publication, page 46, line4-6, in particular).

16. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/44106 (Oct 8, 1998; PTO 1449) in view of US 6,083,713 (July 2000, PTO 892).

The teachings of the WO 98/44106 publication have been discussed supra.

The claimed invention in claim 13 differs from the reference only that the method wherein targeted drug delivery system is a lissome coated with antibody that specifically targets neuronal tissue.

The '713 patent teaches liposomes are well known examples of delivery vehicles for hydrophobic drug (See column 23, lines 26-28, in particular) and one may administered *any* drug in a targeted drug delivery system by liposome coated with a neuronal specific antibody so that the liposome will be targeted to and taken up selectively by the neuronal tissue (See column 24, lines 15-20, in particular). The advantage of local administration or selective uptake increases the effective local concentration of the drug and not related to plasma concentration that is associated with systemic toxicity (See column 24, lines 21-23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to target any drug as taught by the '713 patent for a method of treating a neurological disorder in human patient which comprises administering to said human patient an effective amount of a polypeptide comprising a sequence substantially equivalent to SEQ ID NO: 2 by liposome coated with neuronal specific antibody as taught by the WO 98/44106 publication and the '713 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '713 patent teaches liposomes are well known examples of delivery vehicles for hydrophobic drug (See column 23, lines 26-28, in particular) and one may administered *any* drug in a targeted drug delivery system by liposome coated with a neuronal specific antibody so that the liposomes will be targeted to and taken up selectively by the neuronal tissue (See column 24, lines 15-20, in particular). The advantage of local administration or selective uptake increases the effective local concentration of the drug (See column 24, lines 21-23, in particular).

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

19. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
January 13, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600